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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/485,583	02/14/2000	KOICHI ENDO	ENDO=12	5957

7590 07/28/2004

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WASHINGTON, DC 20001

EXAMINER

MITCHELL, GREGORY W

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/485,583

Applicant(s)

ENDO ET AL.

Examiner

Gregory W Mitchell

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8, 9, 12-14, 19-23 and 27 is/are pending in the application.
- 4a) Of the above claim(s) 12-14 and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8, 9, 22, 23 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 4, 2004 has been entered. Claims 8, 9, 12-14, 19-23 and 27 are pending, of which claims 12-14 and 19-21 have been withdrawn from consideration.

Receipt is acknowledged of Amendments filed on April 5, 2004 and May 4, 2004. Claim rejections made under 35 U.S.C. 112(2) as indicated in the Office action dated November 11, 2003 are hereby withdrawn. Claim rejections made under 35 U.S.C. 103(a) in the previous Office action are also withdrawn. The following new rejections are made:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8, 22 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Moore et al. (J. Med. Chem. 37, 3886-8).

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Moore et al. teaches the use of the selective iNOS inhibitor L-N-(1-iminoethyl)lysine in animal models of disease, such as adjuvant arthritis and glomerulonephritis. As evidenced by Osterman et al. (Inflammation Research, 46, 79-85, see abstract) and Rose et al. (La Presse Medicale, 16, see abstract), both adjuvant arthritis and glomerulonephritis, respectively, are known to be associated with bone resorption. Moore et al. discloses that the ratio of the IC50 level on cNOS compared to that on iNOS is 28 for the iNOS inhibitor L-N-(1-iminoethyl)lysine. The effective dosage taught by Moore et al. for iNOS inhibition was from about 0.2 μ M to 100 μ M. Applicant's specification teaches on page 12 dosages of 0.1 or 0.2 mg/kg which, assuming a density of 1.0 g/mL, is equal to dosages of 0.5 μ M and 0.1 μ M, respectively. Because Moore et al. teaches the same concentration of the selective iNOS L-N-(1-iminoethyl)lysine given to the same population, an animal suffering from one of the afore mentioned bone resorption diseases would inherently be treated for those diseases.

Examiner takes the position that the phrase "as a bone mass-maintenance drug to maintain bone mass" is merely a recitation of intended use, i.e. the reason for "treating a bone resorption-associated disease" with an iNOS inhibitor, and no additional weight is given thereto.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 9 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. as applied to claims 8, 22 and 27 above, and further in view of Hukkanen et al. (Endocrinology, 136, 5445-53).

Moore et al. applies as disclosed above. Moore et al. does not teach the administration of an iNOS inhibitor to an animal suffering from the specific disease associated with bone resorption, osteoporosis.

Hukkanen et al. teaches that iNOS inhibitors inhibit the effects of cytokines in general. The cytokines listed in Hukkanen et al. include IFN- γ , IL-6, TNF- α , etc. (See page 5452, first column, first full paragraph). Hukkanen et al. further teaches that TNF- α has an important role in the etiology of bone loss seen in postmenopausal osteoporosis. (See the bottom of p. 5452 and the top of p. 5453).

One of ordinary skill in the art would have been motivated to employ the elected species, L-N-6-(1-iminoethyl)lysine, a selective iNOS inhibitor, in a method of treating osteoporosis because inhibitors of TNF are capable of treating resorption and bone loss in postmenopausal osteoporosis. It would have been obvious to utilize L-N-6-(1-iminoethyl)lysine as a TNF inhibitor for the treatment of postmenopausal osteoporosis because Moore et al. discloses that L-N-6-(1-iminoethyl)lysine is an iNOS inhibitor, Hukkanen et al. discloses that iNOS inhibitors inhibit cytokines (such as TNF- α) and that cytokines, such as TNF, are involved in the etiology of postmenopausal osteoporosis.

One would have been motivated to utilize the selective iNOS inhibitor, L-N-6-(1-iminoethyl)lysine, in a method of treating postmenopausal osteoporosis because of an

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expectation of success in treating bone loss with selective iNOS inhibitors in general and with L-N-6-(1-iminoethyl)lysine, specifically.

Response to Arguments

Applicant's Amendment filed April 5, 2004 has necessitated the withdrawal of all 35 U.S.C. 112(2) rejections as the rejections were drawn to now cancelled claims.

Applicant's arguments, filed April 5, 2004, with respect to the rejection(s) of claim(s) 8, 9, 22 and 23 under 35 U.S.C. 103(a) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Moore et al. (J. Med. Chem. 37, 3886-8), Hukkanen et al. (Endocrinology, 136, 5445-53).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory W Mitchell whose telephone number is 571-272-2907. The examiner can normally be reached on M-F, 8 AM - 4 PM.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory W Mitchell
Examiner
Art Unit 1617

gwm



SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER